Fact Sheet: 12-dose Isoniazid (INH)/Rifapentine Regimen for Latent TB Infection Treatment

NOTE: It is <u>imperative</u> to rule out active disease in all persons prior to initiating treatment for LTBI

How many are infected with tuberculosis?
In California, an estimated 2.3 million people have tuberculosis (TB) infection. In 2011, 2,317 persons were diagnosed with TB disease in California. An essential element of TB control is the treatment of latent TB infection (LTBI).

What is the 12-dose INH/rifapentine regimen?
It consists of 12 once-weekly doses of INH and rifapentine administered by directly observed therapy (DOT) for the treatment of LTBI.

Is the regimen effective?
A randomized controlled trial* showed that the 12-dose regimen administered by DOT is as effective as 9 months of daily INH self-administered therapy (SAT) for LTBI treatment. The 12-dose regimen was more likely to be completed when compared to 9 months of daily INH.*

What are the advantages of this regimen?
- The 12-dose regimen reduces treatment time by two-thirds (from 9 months to 3 months)
- Weekly dosing offers convenience for some groups
- Higher rates of treatment completion
- Lower rates of hepatotoxicity

Does CDC recommend this regimen?
The 12-dose regimen is recommended as an equal alternative to 9 months of daily INH by SAT for treating LTBI in otherwise healthy persons aged 12 years or older.

Who should be considered for treatment with the 12-dose regimen for LTBI?
- Healthy persons 12 years or older
- Recently exposed contacts to infectious TB and new TB test converters
- Persons with radiographic findings of healed pulmonary TB (e.g., fibrotic disease)
- HIV-infected persons who are NOT taking antiretroviral medications

Are there others to consider for treatment using the 12-dose regimen?
The regimen can be considered on a case-by-case basis for persons not included in the study, such as persons with a co-existing medical condition (e.g. diabetes mellitus, on immunosuppressive therapy) and children aged 2–11 years.

Who is *<u>NOT</u>*** recommended for treatment with the 12-dose regimen?**
- Children under 2 years of age
- HIV infected persons taking antiretrovirals (there are potential drug interactions with rifapentine and antiretrovirals)
- Persons presumed infected with *M. tuberculosis* resistant to INH or rifampin
- Pregnant women or women planning to become pregnant during treatment
- Individuals who have had prior adverse events or hypersensitivity to INH or rifampin

What are the doses?

Drug	Dosage	Maximum dose
INH	15 mg/kg rounded to nearest 50/100mg	900 mg
Rifapentine	10.0 – 14.0 kg = 300 mg	900 mg
	14.1 – 25.0 kg = 450 mg	
	25.1 – 32.0 kg = 600 mg	
	32.1 – 49.9 kg = 750 mg	

What is completion of therapy?
Completion of therapy is defined in the study as completing at least 11 weekly doses of treatment within 16 weeks. Doses should be given at least 72 hours apart.

Does this regimen have to be administered via DOT?
- CDC recommends DOT for this regimen
- A CDC-sponsored trial is underway to investigate the efficacy with SAT

How frequently were toxicities observed in the 12-dose regimen in the clinical trial participants?

- Possible hypersensitivity (3.8%)
- Rash (0.8%)
- Hepatotoxicity (0.4%)
- Thrombocytopenia (infrequent)
- Other toxicities (3.2%)

Note: Please refer to product insert for full list of side effects.

What can a hypersensitivity reaction include and how should I respond?

Hypersensitivity reactions may include a flu-like syndrome (e.g. fever, chills, headaches, dizziness, musculoskeletal pain), thrombocytopenia, shortness of breath or other signs and symptoms including wheezing, acute bronchospasm, urticaria, petechiae, purpura, pruritus, conjunctivitis, angioedema, hypotension or shock.

- If moderate to severe reaction (e.g., thrombocytopenia, hypotension), hospitalization or life-threatening event
  ⇒ *Discontinue treatment*
- If mild reaction (e.g., rash, dizziness, fever)
  ⇒ *Continue to monitor patient closely with a low threshold for discontinuing treatment*

How do I report an adverse event regarding the 12-dose regimen?

All adverse events should be reported to FDA MedWatch, https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm

- Report adverse events leading to death or hospitalization to the local health department, who will report to the CDPH TB Control Branch (TBCB). TBCB then reports to the CDC.

Are there drug-drug interactions?

- INH increases blood levels of phenytoin and disulfiram
- Rifapentine decreases blood levels of oral contraceptives, warfarin, sulfonylureas, methadone, steroids, some cardiac medications, and some antibiotics including fluoroquinolones
- Rifapentine has interactions similar to rifampin; it induces cytochromes P4503A4 & P4502C8/9 (less than rifampin)

Note: Please refer to product insert for full list of drug-drug interactions.

What type of monitoring do I need to do?

- Monthly interview and brief physical examination to identify treatment-associated adverse events
- Baseline hepatic chemistry is recommended for patients with specific conditions:
  - HIV infection
  - Liver disorders
  - In the immediate postpartum period
  - Regular alcohol use
  - Consider also for older persons and those taking medications for chronic medical conditions
- If baseline hepatic chemistry testing is abnormal, continue with subsequent testing

What is the *approximate* monthly public health pricing cost of the 12-dose regimen?

Rifapentine & INH	$ 54.00 + $1.00
Monthly clinic visit	$ 26.00
DOT	$ 96.00
TOTAL	**$177.00 monthly**

How do I obtain Medi-Cal reimbursement?

- Use the ICD-9 code 010.10.96 for primary tuberculosis infection
- Rifapentine is reimbursed at approximately $20.00 per 900 mg dose
- DOT is reimbursed at approximately $19.00 per encounter
- Instructions for Medi-Cal DOT reimbursement www.medi-cal.ca.gov

How do I get rifapentine for my program?

Rifapentine can be ordered from your distributer or wholesaler, or directly from the manufacturer, Sanofi-Aventis, at www.sanofi.us and can be found in the “other products” link.

For questions or assistance in accessing rifapentine, contact the TB Control Branch at 510-620-3000.

Resources

California Department of Public Health
Tuberculosis Control Branch (TBCB)
http://www.cdph.ca.gov/programs/tb/Pages/default.aspx
510-620-3000

California TB Controllers Association
http://www.ctca.org/
510-479-6139

FDA MedWatch
https://www.accessdata.fda.gov/scripts/medwatch/medwatch-online.htm
888-463-6332

Centers for Disease Control and Prevention
Division of Tuberculosis Elimination
http://www.cdc.gov/tb/
800-232-4636

Curry International Tuberculosis Center
Warmline Consultation Service
http://www.currytbcenter.ucsf.edu/
877-390-6682 **or** 415-502-4700

References

Centers for Disease Control and Prevention. (2011). *Recommendations for use of an isoniazid-rifapentine regimen with direct observation to treat latent mycobacterium tuberculosis infection. (*MMWR Vol. 60 No. 48). Georgia: U.S. Department of Health and Human Services.

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*Sterling, T., Villarino, M., Borisov, A., et al. (2011). Three months of rifapentine and isoniazid for latent tuberculosis infection. *The New England Journal of Medicine, 365*(23). 2155-2166.